

SPECIFICATION AMENDMENTS

Replace the Title with:

--PHARMACEUTICAL PRODUCT COMPRISING TRANSGENIC POLLEN
EXPRESSING HETEROLOGOUS POLYPEPTIDES—

Amend the Specification by:

Page 11, prior to the heading “Detailed Description of the Invention” on line 1, add the following section:

--Brief Description of the Drawings

Figure 1 is a schematic representation of the binary plasmid pPvchit Δ 1200gus, used as vector for the reporter gene GUS under the control of part (-1200) of the bean chitinase promoter.

Figure 2 is a photograph of a tobacco flower, clearly showing the anthers.

Figure 3 are counts of mononuclear cells A), neutrophils B), and eosinophils C), in alveolar lavage (BAL) of rats subjected to three consecutive instillations of pollen grains in the indicated concentrations and in pleural lavage of rats subjected to intrapleural injections of pollen grains in the same concentrations. □ and ■ represent, respectively, the average values of BAL and pleural controls. C), D), and F) represent, respectively, the counts of mononuclear cells, neutrophils and eosinophils of broncho-alveolar lavage of rats subjected to three consecutive instillations of WT or GM pollen grains in the indicated concentrations. Dashed lines represent the average values of the controls instilled with saline solution. Columns represent averages \pm E. P. M. and asterisks indicate statistically significant differences ($p < 0.05$).

Figure 4 is a schematic representation of binary plasmid pCambia 1303, used as vector having the reporter genes GFP, GUS and of the selection markers for Kanamycin

and hygromycin. Single restriction sites *Xba*I and *Nco*I and other single and double restriction sites are also indicated.

Figure 5 is a schematic representation of the binary plasmid pCambia 1303 without the CaMV 35S promoter region, as per the cleavage with *Xba*I and *Nco*I enzymes.

Figure 6 is a schematic representation of the ProAtGRP67 region obtained by PCR and the fragment ProAtGRP17 generated by cleavage with *Xba*I and *Nco*I enzymes. In the latter the shorter arrow indicates the relative position of exon 1 and the intron.

Figure 7 is a schematic representation of the plasmid pProAtGRP17_GUSGFP, resulting from the cloning of the PCR product ProAtGRP67 cleaved with *Xba*I and *Nco*I in the plasmid pCambia 1303 cleaved with the same enzymes. The 616 bp region corresponding to the part of the AtGRP17 promoter region and the AtGRP17 gene ORF are indicated as ProArGRP17. Reporter genes GUS and GFP are also indicated.

Figure 8 shows 1% agarose gel containing the expected DNA fragments of the plasmids extracted from transformed *E. coli* XL1, obtained after cleavage with the indicated enzymes. 1, pCambiaProAtGRP17 *Pvu*II; 2, pCambiaProAtGRP17 *Bgl*II; 3, pCambia *Pvu*II; 4, pCambia *Bgl*II; 5, 1kb ladder marker.

Figure 9 shows floral structures of *A. thaliana* transformed with the plasmid pCambiaProAtGRP17GUSGFP. Panel A) shows the presence and activity of GUS on the late anthers' development, but not in the initial stages of development. Panel B) shows inflorescences of the same plant in which the activity of GUS can be seen in the anthers of immature flowers (left) and in the anthers and petals of the mature flower (right). Panel C) shows intense GUS activity on the tapetum and on the pollen grains. Panel D) shows a pollen grain with positive stain for GUS. All photographs were taken under an optical microscope.--

Page 36, line 14 – page 37, line 3, amend the paragraph as follows:

In order to fulfill these requirements, in one of the preferred embodiments of the present invention, the coding gene of the heterologous polypeptide in question is translationally fused to the coding sequence of the AtGRP17 gene (SEQ 1), while said fusion is controlled by at least part of the promoter region (SEQ 2) of the AtGRP17, this promoter being able to direct the gene fusion expression in the anther's tapetum. In order to prepare said gene construction, the following steps were taken:

For the amplification of the promoter region of the AtGRP17 and its ORF specific oligonucleotides were used: RR1f (5'ATA AAG CTT TTT CTC TGT TTT TGT CCG TGG AAC) (Seq. 3) and RR2r (5'ATA CCA TGG CAC GTG ATT CGG TGG AAG TCC TGC C) (Seq. 4). The plasmid pC027 (described by Olivera et al "Inflorescence-specific genes from Arabidopsis thaliana encoding glycine-rich proteins". Plant J. 3: 495-507,1993 ; Franco et al., "Distal regulatory regions restrict the expression of cis-linked gene to the tapetal cells". FEBS Letters 25965: 1-6, 2002) was used as target for the amplification, by PCR, of the promoter region and of the AtGRP17 ORF. By using the oligonucleotides RR1f and RR2r the product of amplification ProAtGRP67 (Figure 6) was obtained and, after cleavage with the enzymes *Xba*I and *Nco*I, was linked to plasmid pCambia cleaved with the same enzymes (Figure 5), thus originating the construction pProAtGRP17_GUSGFP (Figure 7).